A. There's an animal study I have here that was three days. There's a dog study that I have, there was a sample drawn three days.

Q. For blood?

A. No. Well, I know vitreous was involved, but I don't know if blood was involved.

Q. While you are looking for that, is three days a really long time to wait to draw postmortem samples?

A. Yes.

Q. Is two days a really long time to wait?

A. Well, it's long the way I look at it, but it happens.

No, I'm sorry, this -- the three days in the dog study was only for eye tissue, it was not for blood.

Q. Okay.

A. I mean, there are autopsies that we have seen that have been done two days after death. So, I mean, obviously the sooner you get a sample, the better it is. But we see them.

Q. All right. I know you see it, but would you agree with me that the level of postmortem redistribution in heart blood of digoxin is likely to be substantially more at 24 hours than it would be at

five hours?
A. Absolutely.
Q. Would you agree that it would likely be substantially more at 44 hours than it even would be at 24 hours?
A. Probably.
Q. The sample here, was it frozen when NMS received it?
A. No.
Q. And it was whole blood, correct, not serum?
A. It was not serum, no. It was whole blood.
Q. Are digoxin concentrations in whole blood typically higher than in serum?
A. The literature says the ratio between serum and -- or blood to plasma ratio, for example, is about 1 to 1.1. So they are pretty close.
Q. By the way, in the literature that you reviewed, is there any -- did you see any estimate of the amount of digoxin concentration in heart tissue versus blood?
A. Yeah. There's one study that has -- Baselt lists some general information about heart tissue versus blood.

Q. Is it 30 to one?
A. That's a close estimate.
Q. What does that tell you as a forensic toxicologist about the potential for postmortem redistribution of that drug between heart tissue and the blood?
A. Well, the potential is very good it's going to have PMR.
Q. But does it tell you anything about the magnitude of PMR?
A. No.
Q. So could it be as high as 30 times? Is that potential?
A. Well, I guess on a theoretical basis if you have two compartments where one concentration is 30 times greater than the other, you have to come to some equilibrium.
There's a theoretical potential of that. I don't know if I have ever seen anything like that occur.
Q. Okay.
A. I mean, even with the most -- like tricyclic antidepressants, which are the classic group of compounds for PMR, I think the highest number I've ever seen is 15, which is rare. Certainly not an

average.

Q. All right. Certainly a postmortem blood specimen drawn 44 hours after death could very likely redistribute on a magnitude of ten times, correct?

A. I don't know that.

Q. All right.

A. I haven't seen any papers that describe the kinetics of redistribution in humans like that.

So I don't know when the final equilibrium would be reached, and whether 44 hours is -- you know, it's still redistributing and whether it goes up to ten times. I just don't know.

Q. You don't have an opinion either way?

A. I don't. I mean, I could talk about averages, but I don't know what the ranges would be.

Q. Just so I'm clear, the longer you wait after death to draw the blood sample, the more likely it is that there will be postmortem redistribution, correct?

A. That's fair.

Q. Including for digoxin?

A. That's fair. Again, eventually you are going to reach an equilibrium, and there will be no change after that. But, yeah.

Q. But you don't know where that

equilibrium point is?
A. No, I don't.
Q. Could it be higher than ten times?
A. The PMR distribution?
Q. Yes.
In other words, a magnitude of ten times.
A. Well, I mean, the average is around two. I mean, the literature average is around two.
But I'm sure there are cases that it could go that high. Again, I don't know.
Q. Okay. Well, I asked you earlier about that Clarke reference, and you agreed that concentrations of some drugs could increase by as much as two to tenfold after death in postmortem blood.
A. Well, I know that that's true for trtricyclicsicylics, so some drugs including tricyclics. Digoxin specifically, I don't know.
Q. Have you seen any literature specifically on digoxin which discusses the magnitude of the PMR?
A. No.
Q. Bear with me a minute here.
A. Yes, of course.
Q. Okay. In your own stack I believe you

have Vorpahl's article?

A. Yes, I do.

Q. Go to page 333 of that article.

A. Okay.

Q. Actually go to page 332, first of all. Second paragraph on 332. Third paragraph, I'm sorry, on 332. It starts with Although.

A. Um-hum.

Q. Although the vitreous concentrations also differed markedly from true antemortem concentrations, they were more accurate indicators of toxicity.

Do you have any experience that leads you to conclude whether you agree or disagree with that statement?

A. No. That's just a statement that they made.

Q. Okay. Let's go to 333, please.

First sentence under Discussion. It says: It is clear from this investigation that postmortem digoxin levels taken from cardiac blood, venous blood or vitreous humor do not mirror the antemortem levels.

Do you agree with that?

A. Yes.

Q. Substantial increases in the serum levels occur following death irrespective of the source of the sample.

Do you agree with that?

A. Yes.

Q. Now, do you know who Dr. Koren is?

A. Gideon Koren?

Q. Yes.

A. Yes, I've heard of him.

Q. Is he a reputable toxicologist?

A. I think he's a clinical toxicologist. He's up in Toronto, I believe.

Q. Yes.

A. I'm familiar with his work on cocaine and alcohol abuse in pregnant women.

Q. Have you ever read any of his work on digoxin?

A. No.

Q. I would like you to go to -- can I see that article?

A. (Handing article.)

Q. Okay. You can chuck those, because it's the wrong article.

And I'm going to read to you from another Koren article. It says here -- this is an

article by Koren in the American Journal of Cardiology published in April of 1985.

It says: An attempt to prove digoxin intoxication as a cause of death may be hampered by the fact that the postmortem levels may be 1.5 to ten times higher than antemortem levels.

Consequently, one cannot readily use these postmortem data to predict antemortem concentrations.

Do you agree with that?

A. I can't agree or disagree. That's a statement he's making based on that research or it's just discussion, I don't know.

Q. Okay. Have you ever seen any articles published in the peer-reviewed medical literature to indicate that digoxin does not redistribute postmortem as high as ten times?

A. I haven't seen articles that say either way.

Q. Okay. I'm going to hand you this article.

(Discussion off the record.)

BY MR. MORIARTY:

Q. Have you ever read this article?

A. Yes, many years ago.

Q. By Drummer?
A. Um-hum.
Q. It's published in the Therapeutic Drug Monitoring.
Do you see that?
A. 2002.
Q. Is that a publication you subscribe to or review?
A. Well, I read articles, but I don't have a personal copy of it. We get it here.
Q. Okay. Let's go to page 206. Second column under Redistribution, towards the end of the first paragraph.
It says: Changes in concentration up to tenfold in cardiac blood are known when compared with specimens taken antemortem or shortly after death.
A. I'm sorry. Can I stop you?
Q. Sure.
A. Page 206?
Q. Yeah. I'm sorry, 205.
A. Thank you.
Q. 205 under Redistribution.
A. We are on the same page now, okay.
Q. It says: Changes in concentration up to tenfold in cardiac blood are known when compared with

specimens taken antemortem or shortly after death. The drugs most affected include digoxin.

And then it goes on to others, including the tricyclics that you referred to earlier.

Do you agree with that?

A. I trust that Dr. Drummer is producing this accurately.

Q. Okay. And then on 206, second column, right here.

A. Okay, I see it.

Q. Do you see that?

It says: Cardiac blood is not in general a suitable sample for quantitative analysis.

Do you agree with that?

A. Yes. In terms of producing drug concentrations that are circulating, yes.

I mean, we can use concentrations in cardiac blood to tell us something, but not for certain purposes.

Q. And those purposes would be for back calculating either the antemortem serum digoxin level or the dose taken before death?

A. Well, or to give an estimate of what -- to the medical examiner or the coroner as to what the circulating level might be.

Q. Do you ever read the British Journal of Clinical Pharmacology?

A. Rarely. At present, I should say. Years ago I did.

Q. Have you ever read this article?

A. No, I have never seen this.

Q. By Ferner?

A. No, I haven't seen it.

Q. I would like you to go to page 430.

A. The first page?

Q. Yes, sir.

In the abstract itself, the second sentence: Postmortem changes render the assumptions of clinical pharmacology largely invalid and make the interpretation of concentrations measured in postmortem samples difficult or impossible.

Do you agree with that?

A. Not necessarily. That's his opinion.

Q. Okay. Let's go to page 440, under Conclusion.

It says: There is no reliable or obvious connection between concentrations measured in life and subsequent to death.

Consequently, concentrations measured after death cannot generally be interpreted to yield

concentrations present before death.

Do you agree with that?

A. That's a very broad statement. And there are times when you can make those conclusions, and there are times when you cannot.

Q. Okay.

A. So I would say I can disagree in certain circumstances and others I would not.

Q. All right. Would you agree that that is true in digoxin generally?

A. Again, there's a timing issue here.

Q. All right.

A. So the answer to your question is I'm not sure.

Q. Would you agree in a digoxin case in which the postmortem sample was heart blood drawn 44 hours after death?

A. I think it certainly would be a less reliable indicator, absolutely.

Q. All right. Now, in a living patient do you know the optimum time for drawing a serum digoxin concentration?

A. The recommendation is six hours.

Q. In this case do you know when Mrs. Johnson took her last dose in regard to her

death?

A. I don't have specific information, no.

Q. Is that a variable you would need to know if you were going to render an opinion about whether a postmortem specimen was meaningful or not?

A. That would certainly be helpful information, absolutely.

Well, can I go back? When you say "a postmortem specimen was meaningful," you mean the concentration found in this?

Q. Yes.

A. Yes.

Q. Do you have an opinion to a probability in this case whether this postmortem blood level of 18 nanograms per milliliter can be used to reliably back calculate her antemortem serum digoxin concentration?

A. Not with the facts I have presently.

Q. All right. Do you have an opinion to a reasonable degree of probability as to whether this postmortem blood specimen of 18 nanograms per milliliter can be used to reliably back calculate her predeath dose?

A. I would say that would be a very tentative assumption. It would probably not be that reliable.

Q. Let's talk about vitreous samples for a second. This is page 96 of Clarke's text. By the way, this is from the third edition, all right.

In that section it says: Vitreous humor has also been used increasingly for the measurement of drugs.

You agree with that, correct?

A. Yes.

Q. For example, digoxin concentrations increase markedly in postmortem cardiac blood, but do not increase significantly in vitreous humor.

Did I read that correctly?

A. You did.

Q. And they refer there to the Vorpahl and Coe article in 1978 that you actually have here today, correct?

A. Yes.

Q. Now, do you agree with that statement?

A. Well, that's based upon that original work by Vorpahl and Coe, but they use vitreous at one point in time. They didn't do any measurement over a period of time.

Q. Understood.

A. So, I mean, there's nothing wrong with that statement as he cites that reference.

Q. I'm asking whether you agree with that statement as of today, not just in relationship to Vorpahl and Coe.

A. Well, no. Vitreous levels do increase over time in postmortem situations.

Q. Their statement is: Therefore, vitreous digoxin concentrations give a better indication of perimortem concentrations than does heart blood.

Do you agree with that?

A. Not necessarily. There are people who ascribe to that. But I think as we're learning more we see that there are problems with vitreous levels as well as heart blood levels or any other peripheral sample level.

Q. All right. So, based on -- now the vitreous level for Mrs. Johnson's sample was what, 1.5, right?

A. That's what was reported, yes.

Q. And the common therapeutic range of digoxin in antemortem specimens is .8 to 2 nanograms per milliliter?

A. Serum levels, yes.

Q. Serum levels.

A. Yes, that's correct.

Q. So based on this vitreous sample, are

you going to render any opinion to a probability as to what Mrs. Johnson's antemortem serum digoxin level was?

A. No.

Q. What about her antemortem dose?

A. No. Not with the information that I have right now. There's no way.

Q. Just based on the information that you have here, where you have got cardiac blood at 18 nanograms per milliliter and vitreous at 1.5 nanograms per milliliter, isn't it more likely than not that the antemortem SDC, if drawn, would have been under two?

A. Why would you say that?

Q. I'm asking you.

A. No. I don't see the connection.

Q. Okay. Is there any published scientific literature to indicate that postmortem vitreous samples of digoxin decrease in their levels after death?

A. We're talking human now. No. I don't believe I've seen any literature that suggests that.

Q. Is there any in animal models?

A. There's a guinea pig model which shows that over a period of time the vitreous level will change.

Q. Change up or down?
A. Decreasing.
Q. Decreasing.
A. Decreasing.
Q. How many tests did they run? I guess, how many guinea pigs did they use?
A. It was a small number.
Q. Did they say how much it decreased?
A. No. They gave some parameters. And this has to do with an intravenous administration, so we could be talking about a redistribution issue too.
For example, this is an article that I have in my package, Journal of Toxicology, 1991, by Donnelly, et al. I'm going to hand this to you in a minute to mark.
And they had administered IV digoxin to guinea pigs and measured levels of serum and vitreous over time. And the levels decreased -- this is in minutes -- the first sampling at 15 minutes was over 10 nanograms per mil.
MS. AHERN: I'm sorry. Was that vitreous?
THE WITNESS: This is vitreous.
MS. AHERN: Okay, thank you.
THE WITNESS: Ten nan -- over 10, it

looks like about 15, and at 480 minutes it was down around a little bit over one. So it decreased about ten times.

But, of course, that could be a distribution.

But to answer your question, that would be an article that could answer the question you just asked.

BY MR. MORIARTY:

Q. And when you say it might have been a distribution, I don't know what you mean by that.

A. Well, digoxin -- because you asked me before about drawing serum levels. It takes about six hours for the recommendation of drawing the serum level.

This is because digoxin does have a slow distribution. It takes many hours for it to redistribute.

So the kinetics in a living individual show that you have a distribution phase that you want to get to a steady state, and have the elimination phase before you're doing anything.

And so this is certainly an acute administration of the compound, but the levels would decrease. And so that just could be a matter of

distribution.

They don't specifically talk about that because it's a very different kind of model.

Q. If I understand what I think you are saying the, IV administration of digoxin to the guinea pig was close in time to when they were then sacrificed and the vitreous sampled?

A. Exactly. I mean, basically at times zero they administered the drug, and then they measured starting at 15 minutes out to 480 minutes.

Q. That's not a study that you would necessarily -- I mean, that's a different circumstance.

A. Oh, absolutely. I was just trying to answer your question --

Q. Sure.

A. -- with what you had asked.

(Exhibit No. Barbieri 7, Comparative Kinetics of Serum and Vitreous Humor Digoxin Concentrations in a Guinea Pig Model. Part I: Intravenous Administration of Digoxin, marked for identification.)

BY MR. MORIARTY:

Q. And the article that you just mentioned I've marked as Barbieri No. 7. Is that correct?

A. That's fine, yes.
Q. So, if I understand what you are telling me in general, based on the information you have today, you are not going to be rendering any interpretation to a reasonable degree of scientific probability or certainty regarding Mrs. Johnson's predeath dose or serum levels based on the vitreous and/or the blood analysis done by NMS, correct?
A. That's correct.
Q. Can I see the other articles that you brought? Because I want to clean this up.
A. These were yours that you gave to me, the ones that were over here.
(Exhibit No. Barbieri 8, Post-mortem Clinical Pharmacology, marked for identification.)
(Exhibit No. Barbieri 9, Postmortem Drug Analysis: Analytical and Toxicological Aspects, marked for identification.)
BY MR. MORIARTY:
Q. The British Journal of Clinical Pharmacology article I asked you about I've had marked as Exhibit 8. Is that correct?
A. Yes, I see that.
Q. And the Therapeutic Drug Monitoring article from 2002 that I asked you about is Barbieri

No. 9. Is that correct?

A. I see that, yes.

Q. Now I'm in the stack that you handed me from your own file.

This one on top, is this from Goodman and Gilman's?

A. No. That's from Baselt. That's the 8th edition of Baselt. I'm sorry, I should have printed the front page.

Q. This article that you pulled by Holmgren in the Journal of Forensic Sciences, was this only about the stability of samples?

A. Yes. When I went in to the Internet, it indicated that that was -- that had some information on digoxin. It does not.

Q. Okay.

A. So I read through it anyway, so I just included it.

Q. All right. And just for the record, that's July of 2004, correct?

A. Yes.

Q. And then you have Dr. DiMaio's article from the Journal of Forensic Sciences in April of 1975. Is that correct?

A. Yes.

Q. Then this is a Journal of Cardiovascular Pharmacology from 1980: Digoxin in the optic tract in digoxin intoxication.

A. Yes. Binnion and Frazer. This is the dog study that I referred to earlier.

MR. MORIARTY: I'm going to mark this one. I'm up to 10, right?

(Exhibit No. Barbieri 10, Digoxin in the Optic Tract in Digoxin Intoxication, marked for identification.)

BY MR. MORIARTY:

Q. I marked that one Exhibit 10, correct?

A. Yes.

MR. MORIARTY: And then let's see if I could do this one.

(Exhibit No. Barbieri 11, Measurement of Digitalis-Glycoside Levels in Ocular Tissues: A Way to Improve Postmortem Diagnosis of Lethal Digitalis-Glycoside Poisoning marked for identification.)

BY MR. MORIARTY:

Q. I marked as No. 11 Measurement of Digitalis-Glycoside Levels in Ocular Tissue, and then there is an Article No. 1 and Article No. 2, correct?

A. Yes.

Q. By the same authors?

A. Yes. The first is for digoxin, the second is digitoxin, which is a different --

Q. Different compound.

A. Totally different kinetics, different drug.

Q. I'm going to put these in and count them all as Exhibit 11, fair?

A. Fair.

Q. And the last one that was in your file is Comparative Kinetics of Digoxin and Serum and Vitreous Humor in a Guinea Pig Model, correct?

A. Is this Part 1 or 2? I think Part 1, we had talked about the intravenous already, and that should be oral dose. Is that the one you have?

Q. Where is that exhibit?

MR. MORIARTY: Hunter, do you have that?

MS. AHERN: No.

MR. MORIARTY: Oh, here we go.

BY MR. MORIARTY:

Q. So we talked about Exhibit 7 earlier, correct?

A. Yes, that's correct.

Q. And then what is this article?

A. That's a related article, but that's an oral dosing study, also in guinea pigs.

MR. MORIARTY: All right. Then I'm going to mark this one separately as No. 12.

(Exhibit No. Barbieri 12, Comparative Kinetics of Digoxin in Serum and Vitreous Humor in a Guinea Pig Model. II. Single Oral Dose Administration, marked for identification.)

BY MR. MORIARTY:

Q. And do you know whether the oral dosing study reached any conclusions different than the IV dosing study about PMR of digoxin either in the heart or the ocular tissues?

A. Well, it doesn't show that there's a significant decrease over time as the intravenous one did in the ocular tissues.

Q. And of course in humans in an outpatient situation it's oral dosing, correct?

A. In an outpatient situation, yes. I mean, I'm sure occasionally there's an intravenous given, but it's not common.

MR. MORIARTY: Why don't we take a five-minute break. I want to get all of this stuff together and confer with my colleagues.

THE WITNESS: Okay.

(A recess is held.)

BY MR. MORIARTY:

Q. Now, when you had your meetings with Mr. Miller and Mr. Deligans back some time in September, I think you said it was over the telephone, did you tell them at that time that you could not to a probability extrapolate back to calculate her predeath -- Mrs. Johnson's predeath dose or serum digoxin concentration?

A. I don't think we talked about that.

Q. Did you tell Mr. Miller that when you met with him yesterday?

A. That I could not get any kind of exact within a reasonable degree of scientific certainty, yes.

Q. Okay. Do you have interpretative opinions regarding either the vitreous sample of 1.5 or the blood level of 18 to a reasonable degree of scientific probability or certainty?

A. I do have some opinions about them, yes.

Q. Tell me what your opinions are.

A. Let's take the blood data, because I think that's the most significant.

Factoring in the postmortem redistribution and taking the value of two, or even a value of three and dividing that 18 by three, let's say, it would appear to me that at the -- that the

postmortem level factoring in postmortem redistribution was high.

Now, can I say that that was the level that occurred at any point in time? No. That's based upon the measurement that was taken when the blood was drawn.

But obviously knowing a little bit about what I was told yesterday, about the history of the case in terms of her last dose, and trying to calculate going backwards in time from that projected blood level of six, let's say, and the half-life of the compound, which is 30-some hours, you could say that it had to be higher when at least she started getting sick.

So the specifics, no, I can't render any kind of scientific opinion about what her antemortem level was.

But it's obvious to me that it's certainly higher than one would expect after we take postmortem redistribution out of the picture.

Q. What's the basis for that opinion?

A. The basis for that opinion is basically my knowledge of what I know about digoxin's kinetics, PMR; and, again, using average values for postmortem distribution, not using a value of ten, which would

be, you know, exceedingly high and certainly would not be an average value.

Could it occur at that high level? There's always a possibility.

And at the same time there could be a possibility that it could be lower than even two in any particular individual.

Q. Okay. Let me ask you this.

What literature do you use to determine the average PMR levels?

A. Well, the average PMR levels as stated in Baselt's reference.

Q. Which is what?

A. Which says 1.96.

Q. What article was that based on?

A. Let's take a look. Vorpahl and Coe, 1978.

Q. How long was the longest blood draw postdeath in Vorpahl and Coe's article?

A. I think he -- they state 10.8 hours.

Q. Why don't you look at the article, because I thought I saw 22.4 hours.

A. If you could show me that.

Q. I wouldn't be able to find that that quickly.

MS. AHERN: It's the second page, right under results section.

THE WITNESS: Oh, I'm sorry, I was looking at the mean. Yes, thank you for the clarification. Twenty-two hours, 22.4 hours.

BY MR. MORIARTY:

Q. So the mean was what?

A. The mean was 10.8.

Q. All right. So they didn't have any samples 44 hours, did they?

A. No, they did not.

Q. All right. And Baselt's only citing one reference, correct?

A. Yes, that's true.

Q. And that one reference doesn't have any draws as long after death as this one was, correct?

A. Agreed.

Q. All right. So do you know when Mrs. Johnson took her last dose before she died?

A. Based on what I heard --

Q. Yeah.

A. -- about the case?

Q. Yeah.

A. Here's my understanding. I'm not clear on exactly the times, but here's my understanding.

The autopsy was done. She got -- she died approximately 24 hours prior (sic) to her starting to get sick; nausea, vomiting, et cetera, that her husband described.

My understanding is it goes back about -- her last dose was about six hours prior to that. So it would have been -- the time that she died would have been a 30-hour window. Now, the autopsy was done after that, obviously.

That's the information that I was given yesterday, and I believe those numbers are correct.

Q. Well, are you making any assumption of what the dose was?

A. No, none whatsoever.

Q. And your assumption is she took some dose on the morning of the 26th and died on the afternoon of the 27th, correct?

A. Well, again, the specific dates I don't have.

Q. I'm telling you what the dates are.

A. Then I'll take that as a representation, yes.

Q. So it's your understanding she did not take a digoxin dose on the 27th?

A. That's my understanding.

Q. Okay. And I think we covered this earlier, but you don't know her renal status.
A. No.
Q. Don't know her hydration status.
A. I do not, no.
Q. Do you know what other medications she was taking?
A. I do not know that.
Q. Did NMS run the blood specimen or the vitreous for any other drugs besides digoxin?
A. No, we did not.
Q. Were they asked to?
A. We were not asked to do that.
Q. And you are not rendering any opinion about why she had diarrhea on the 26th or 27th, correct?
A. No. I mean, diarrhea can be a toxicity of digoxin. It could also be a pathology from some other cause, or it could be from some other drugs. So I'm not rendering an opinion that that was definitely caused by digoxin.
Q. All right. And there is certainly published literature, excerpts of which I read to you, to indicate the PMR of digoxin can be up to ten times, correct?

A. You read that and people have stated that.
Q. Okay.
A. And certainly that's in the literature.
Q. All right. So what are the other bases of your opinion -- let me withdraw that question.
Are you testifying to a reasonable degree of probability or certainty as to what a range of her antemortem serum digoxin concentration would have been?
A. No, I didn't say that.
As I described to you, what I said was that based upon the level that we measured at the time of collection, and taking postmortem redistribution out of the picture and reducing that number by a factor of three as an example, and then taking the kinetics of the drug, that she's alive over a period of time, that the level had to be higher if she did not take another dose of digoxin as I was told.
Q. Okay.
A. And that's it.
Q. Got it.
And when you say you took PMR into account, you took it as an average?
A. Well, more than the average. I mean,

the average number that I worked with and I've seen is two, and I'm even going to three.

Q. Okay. And there are certainly other published peer-reviewed articles with other numbers of magnitude of PMR?

A. Certainly.

Q. All right. As I understand it, you have no opinion as to what the dose would have been on the 26th that she ingested under the assumptions that you have given me.

A. No. Without having any kind of medical records or medication history I could not opine to that.

Q. All right. Do you know anything about the percentage of cases in which patients have diarrhea as a sign or symptom of digoxin toxicity?

A. I don't have the specifics on that, no.

Q. Do you know whether in Goodman and Gilman's they even mention diarrhea as a sign or symptom of digoxin toxicity?

A. They probably do not; because it's such a common toxicity for drugs, they may not specifically list all the side effects of digoxin.

Q. Well, do you think Goodman and Gilman's, which you keep in your office, would list the more

common side effects?

A. I would say that they would.

Q. Such as arrhythmias, nausea, disturbances of cognitive function and blurred or yellow vision?

A. Yes, that's all true.

Q. Do you know if she had arrhythmias, disturbances of cognitive function or blurred vision?

A. I do not know that, because I have not seen any medical records for her.

Q. Now, let's assume that Mrs. Johnson took her last digoxin dose on the morning of the 26th, okay?

A. Okay.

Q. And she then died, and I think it was at 9:00 in the morning.

Let's just make that assumption, okay?

A. That's when she died?

Q. No. She took her last digoxin somewhere around 9:00 in the morning on the 26th.

A. Okay.

Q. Okay?

From a typical pharmacokinetics standpoint, when would her digoxin level have peaked, serum digoxin level have peaked?

A. From that dose?
Q. Yes.
A. About six hours afterward.
Q. Okay. And then typically what would happen after that?
A. Then the drug -- the distribution would be completed, and so only elimination would take over, and the drug levels would start to fall.
Q. And how much would it fall in -- so if you say six to eight hours after 9:00 a.m., we are out at you know 3:00, 4:00, 5:00 in the afternoon, correct?
A. About 3:00 p.m. is six hours.
Q. Okay. And then let's assume that she died at about 4:00 p.m. the 27th, so there's 24 more hours, correct?
A. Okay.
Q. Isn't it more likely than not that somebody who has a high digoxin level would have their complications around the time when that digoxin level peaked as opposed to 24 hours later?
A. Not necessarily. In most cases you would assume that to be true, but digoxin has a cumulative effect on the heart.
And as the sodium potassium pump is

being inhibited, she could start having, you know, cardiac side effects or cardiac toxicities that are not manifesting itself that she could feel.

And so over a period of time even if her levels start to drop, she could have an arrhythmia at any time; ventricular tachycardia, leading to ventricular fibrillation, leading to sudden death.

That doesn't have to occur at the peak. It could occur at any time during digoxin therapy.

Q. Okay. But typically, in more cases than not, it would occur near the peak?

A. You would expect that a typical dose response would occur.

Q. Okay, sure.

A. But because of the very long half-life of this compound it doesn't have to be.

Q. All right. Have you read any testimony from Dr. Woodson, the treating physician in this case?

A. No, I don't know him, and I have not read anything from him.

Q. Have you been told anything about his opinions?

A. No, I have not.

Q. Do you think that any other forensic toxicologist, based on the data available, could

predict with any more reliable scientific certainty than you have what happened on the 26th and the 27th?

A. I'm sure there's someone who is more versed in digoxin toxicity than I am, or digoxin kinetics than I am, that may be able to do that. I can't answer for everyone.

Q. Okay. Now, when you do testing, you get a specimen, you do testing on it, and then much later down the road you are asked to produce your litigation packets.

NMS typically has all the data on that testing, correct?

A. Yes.

Q. And if NMS did not have the backup data on that testing, what would you tell -- I mean, other than the result page, if you had nothing other than the result page, what would you tell your client about the reliability of that material?

A. Okay, let's take a scenario. We're required to keep all records for a minimum of five years.

So let's say after the fact a case came to trial, and someone was asked to produce a litigation package and all we had was the report.

The report was published, and all we

could say is at the time that this report was generated, all the data were verified by the analysts in the laboratory, the senior scientists or anyone who reviewed that.

And, therefore, we have to stand by the reliability of that data, but we don't have the data because it was destroyed after the five-year period.

Q. Okay.

A. So at the time that it was produced, we feel that all of our data are correct and accurate as produced, unless something comes up afterward and we find an error. If we find an error, we correct that error.

Q. All right. Well, let's just assume it was a year and a half, and for some reason the computer with the data on it, you know, was in a flood or something like that, and that data wasn't available.

Same answer?

A. We would do the same thing.

Q. All right. Certainly the SOFT guidelines contemplate the data be kept and available for analysis, right?

A. Absolutely.

Q. Now, I think earlier in your testimony

you used the word validation several times.

You know what that means, correct?

A. Yes.

Q. And it's universally accepted that methods used in forensic work must undergo validation, correct?

A. In most cases. There are some cases that come up where you have a particular variable or something very specific where you cannot use a validated method.

We will use in generalized scientific principles such as standard addition within the sample itself or other ways in order to verify that the results are accurate and true without having a fully validated procedure.

Q. Okay.

A. But in most of our testing we have validated procedures for the results that we produce.

Q. Before you run tests for an actual client, how long do you typically take to validate a method?

A. It can take anywhere from a couple of weeks to several months.

Q. So how many times would you run and refine a system before you considered it validated?

A. We have a protocol for different things that we do in the validation of an assay. Some things are done quickly.

For example, we can do reporting limits within three runs, let's say, which we normally do, and it may only take three days. We can generate standard curves in that period of time.

If we are doing stability of the analysis in various matrices, we may go out. In fact, right now we go out for 30 days; room temperature, refrigerated, frozen, light protected, non-light protected.

And in some cases we started doing stability studies out to six months or a year.

Q. Okay.

A. Now, we would not hold the validation that long. We would, you know, publish the test and be available after 30 days, let's say; but then we would add to that as we accumulate data over that period of time. So it's quite variable.

Q. All right. For a lab that almost never runs a particular type of test, okay, let's just assume you are running an assay on a solid oral dose form, and it's just not something that your lab typically does or rarely does it.

And the total time from so-called validation to running the standards, the blanks, and the actual sample to be tested was about two to two and a half hours.

Does that sound like a reasonable scientific validated method?

A. That's a difficult question to answer, because I don't know the specifics of what -- you know, what was done.

It seems -- you know, on first blush it seems very short, and it would not be something the way we do it. But it depends upon the resources that were available to that lab.

I'm tending to say it doesn't sound reasonable, but I can't say that with any kind of certainty.

Q. Okay. Let me just ask you a couple more lab-type questions, and then I'll turn this over to some of these other lawyers.

If when you run a blank the intercept is 19,000, what does it do to the reliability of the analysis of the sample?

A. I don't know what that means.

Q. Well --

A. If you are saying a response on the Y

axis would be 19,000 at zero --

Q. Yes, sir.

A. -- so it doesn't go through zero?

Q. Yes, sir.

A. You may have a high noise level that's producing that.

Q. Okay.

A. Or possibly the standard curve is not done appropriately so you don't have a good R-squared value. You may have to use a quadratic fit for that curve.

So there's various reasons for that, but I don't -- it's hard to answer without seeing data.

Q. If the R-squared value is less than .99, how sensitive and specific is the test likely to be?

A. .99 is -- for us it's not great. I don't know how I can answer sensitivity and specificity. I don't know how to answer that question.

Q. What are your R-squares typically here?

A. Minimum three nines. Sometimes four to five nines.

Q. How important is it for the sample to be within the range of the calibrators?

A. Oh, it has to be.

You cannot -- you cannot report a value -- I mean, good science says you cannot a report a value that is over your highest calibrator, or report a value with any certainty that is lower than your lowest positive calibrator; though some people will do that.

They will start at zero and use that as a positive number.

And the reason is because you don't know what happens to the -- you asked the Y in terms of the upper level. You don't know what happens to the curve once you passed your upper calibrator.

Does it flatten out? Does it go exponentially higher? Does it continue to be linear?

So without knowing that, you can't reliably report that elevated value unless you dilute the sample when you run.

Q. Okay. So NMS wouldn't report a result that was higher than the highest calibrator?

A. That's against our SOPs. We do not do that.

Q. Is it against SOFT guidelines?

A. I believe it is in the SOFT guidelines.

Q. SOFT guidelines aren't limited to biological specimens, are they?

A. You know, I haven't read the latest version, and I don't know that. I think probably it's general information, but I don't think it's limited to biologics, no.

Q. Now, you know about LC-MS equipment, don't you?

A. Yes.

Q. All right. In, say, 2009 was commonly used LC-MS equipment capable of calculating down to the 1000th in the decimal system?

A. It depends on the compound we are talking about.

Q. Well, for digoxin, for example.

Could you calculate down to three digits, or would you have to round?

A. You are talking subnanogram per mL? What units are we talking about?

Q. Let's just stick with nanograms per milliliter.

A. Okay. I would be guessing.

Q. That's fine.

Does NMS, when it's doing a solid oral dose testing, typically weigh and/or measure the specimen before it is assayed?

A. We do.

Q. Why?
A. Because that's part of the specimen description that we have.
Q. Do you document the weight and thickness?
A. Well, if we get a tablet, for example, we will weigh that tablet, the single tablet. If we have multiple, we weigh each one.
We'll usually take a photograph of it with a ruler next to it.
So we don't actually document weighing it, but we do things like that.
Q. And then you keep that information available, correct?
A. That's part of the file, sure.
Q. Does NMS sometimes freeze samples?
A. Yes.
Q. Does NMS sometimes thaw samples and retest them?
A. Yes, we have. And we do freeze-thaw experiments in terms of our validation as well.
Q. That's what I was about to ask you.
You validate that process so you know whether the freezing and thawing has an effect on the compound, correct?

A. Yes. Our current validation does three freeze-thaw cycles.
Q. Are those stability studies?
A. They are part of the stability studies.
Q. Is that important to do?
A. Yes. Because we don't know if we were to receive a sample that had been frozen and then thawed; or alternately, we have a sample that we had frozen and then somebody comes back and asks us to do something about it and retest something, we have to thaw it.
So, yes, we need that information.
Q. Did Mr. Miller or Mr. Deligans show you any information about testing done by a lab called ExperTox in this case?
A. No, they did not.
Q. Have you ever heard of ExperTox?
A. I have not.
Q. Do you know anything about their reputation?
A. I do not.
Q. Do you know who Professor or Dr. Ernest Lykissa is?
A. I never heard the name.
Q. So you don't know anything about his

reputation?

A. No, I do not.

MR. MORIARTY: All right. I'm going to let these other lawyers ask you some questions, and then I'll ask you some more at the end if I need to.

EXAMINATION

BY MR. McPHAIL:

Q. Good morning, Doctor.

A. Good morning.

Q. Do we need to take a break or are you ready to keep on going?

A. No, I'm fine, let's do it.

Q. I'm David McPhail. I introduced myself to you before we started. I represent McBride Hospital.

Do you understand that?

A. I know the name McBride Hospital from the notes, but now I know you represent them.

Q. Okay. All right. There are several defendants in this case, but I represent the hospital, and that's the only health care provider that I represent.

A. Okay.

Q. Do you know why McBride Hospital has been sued in this case?

A. No, I do not.
Q. What information do you have related to McBride Hospital?
A. None at all.
Q. You said you saw them in the notes. What do you mean?
A. On the deposition notes and the listings I saw McBride's hospital name here. That's all.
Q. You have seen the name, but you have no understanding whatsoever about why the hospital has been sued in this case?
A. That's correct.
Q. You testify a lot, don't you?
A. Well, it's a relative term, but --
Q. Have you testified more than three times?
A. Yes.
Q. More than 30 times?
A. More than 100 times.
Q. More than 100 times?
A. Yes.
Q. Okay. So would that be inclusive of depositions and trial testimony, or one or the other?
A. Both.
Q. Okay. So how many times have you

testified in front of a jury?

A. I think the information that I provided --

Q. You may have it in detail for me, but just for purposes of our discussion. Just roughly.

More than 50 times?

A. Yes. Let me be specific.

I have listed I think it's about 75 times in a court setting; that may be in front of a jury or bench trial only. And then there were hearings that would not be formal trials again.

And so it's hard for me to sort out. But in total I would say, you know, more than 50 times.

Q. Well, I'll look at your -- the details that you have provided us, and that's fine. But I'm just -- for purposes of our discussion I'm trying to get an understanding.

This is something that you are -- this venue, testifying, providing expert testimony, it's something you are very familiar with, isn't it?

A. Yes.

Q. I take it that you understand that, you know, the purpose of you providing the testimony is to give specialized information about really complicated

subjects to either a judge or a hearing panel or a jury to make a decision in a lawsuit.

A. Yes.

Q. What specialized information do you have that you are, to a reasonable scientific probability, going to be able to offer our jury in this case?

And what I mean by that is, what significant information can you offer this jury that you feel is in any way relevant to this lawsuit?

A. Well, I don't know the specifics of the lawsuit, so that's pretty hard for me to answer the question specifically.

Q. Okay.

A. But basically, I mean, I could testify to what NMS did in terms of testing the samples, the results that we published, the papers that I've read in terms of what digoxin is about, my experience in terms of digoxin as a drug, my teaching experience, et cetera.

Specific to the lawsuit, again there's a lot of information that I don't have, so that's where I'm having difficulty trying to answer your question.

Q. Okay. Let me ask a little more specifically.

At one point during Mr. Moriarty's

questioning -- I tried to write it down pretty closely what it was that he was asking you and you were responding with.

But I thought I heard him say that you were not going to render an opinion as to any antemortem or predeath serum levels or dosing based on any of the information in your litigation packet or any of the testing that NMS did.

MR. MILLER: Objection to form.

THE WITNESS: In terms of being specific, I have tried to do that.

Now later on, as we just came back from the break, I think I tried to explain that I'm not doing anything first in terms of dosing, no, I'm not. In terms of an antemortem level, I can't do that.

BY MR. McPHAIL:

Q. Because nobody can do it accurately?

A. Nobody, right.

Now, as I tried to explain to Mr. Moriarty, what I can say is based upon the concentration I measured, I can make an estimate of saying it's my opinion that the level at the time she started to be sick was high.

But the specific number that we are going to put in terms of therapeutics or not

therapeutics, I'm not -- I can't do that; in terms of especially for an antemortem level at that time.

So I hope I'm being clear there. It's a general ballpark kind of a level. That's all I can do.

Q. Are you finished?

A. I'm finished.

Q. If I step on one of your answers or jump in, hold your hand up or -- I want you to finish, I want you to complete an answer.

Sometimes I get a little bit energized in the discussion here, and I get in a hurry and I don't want to cut you off.

A. That's okay. We all do that, I understand.

Q. The court reporter is staring daggers at me, though, because we are talking on top of each other. And I don't mean to do it, but I'm doing it, and I know I am.

Well, we're in a building.

Do you know how many square feet is in this building?

A. About 65,000.

Q. Okay. And it's got dozens of people in it?

A. Yeah.
Q. And bunches of computers and all kind of high-tech machinery?
A. Yes.
Q. And I think you have said earlier in your deposition that this place, NMS, runs a 1,000 tests a day?
A. That's a ballpark number, yes.
Q. Okay. Well, with all of these people and all of the technology and all of the validation processes and all of the things that we have been talking about, how often do you come in to court and testify in front of a jury based on just some ballpark estimate that you are coming up with in the end?
A. It happen on occasion. Not as common as, you know, you may think. But it does happen on occasion.
Q. Okay. So in the 50-plus times that you have testified in front of a jury that we mentioned earlier, how many of those times are you just giving ballpark opinions as opposed to actually testifying to a number that NMS tested and came up with?
A. Well, in terms of opinions on a case, knowing as much as I can about that case, it happens a handful of times.

Q. Do you feel comfortable doing that, giving just a ballpark opinion, when you have got all the people here and the resources to test all of these samples? I mean, is that something you feel comfortable doing?

A. Well, you are asking me two different things now.

Q. Well, separate it out for me. I don't want to do that.

A. I will. The data that we produce is objective data with a finite number, and so that I testify in terms of what we measured and what we reported, so that's an absolute number. Now, I have absolute confidence in what I do there.

But to give an opinion about retrograde calculations for a simple thing like ethanol, for example, which I do often, that is a ballpark.

Q. And for the understanding of your answer, that's like in a DUI case or some kind of an intoxication case?

A. That would be.

Q. Go ahead, keep going.

A. Retrograde calculations. Or a conversion of a serum alcohol to a blood alcohol, which is what, you know, district attorneys like to

see. I mean, that's the statutes. There are estimates that are being given there.

And I can say within a range, and that's a ballpark, here's what the level would be two hours prior to when the accident occurred, as just as a simple example. So it does happen.

But there's two different things. That's an opinion based upon all the facts of the case that I have, reviewing the data, and coming up with some conclusion and opinion, as opposed to the objective data that NMS produces.

Q. Okay. Have you been asked or do you intend to testify to our jury in this case?

A. I have not been asked to do that.

Q. Would you be willing to do that?

A. Yes, I would.

Q. Would you have to tell our jury in this case that although you are confident in the objective data that NMS has produced from the vitreous and blood sample, that you can't -- you can't use the conclusions reached to reliably tell us anything about her serum levels before she died?

A. If I'm giving testimony, and I have solid objective data that I can be 95 percent confident within a reasonable degree of scientific

certainty, I will state that.

If I'm ballparking or I'm ranging data and I'm unsure of what that means, I will state that.

So in any case, you know, I'm here to produce facts. I'm not here to be an advocate for any side of the case.

Even if somebody hires me. There are many times where I'll tell somebody who hires me, You don't have a case, so I can't help you.

That's my job. So I try to be as honest as possible to the people that I'm speaking to.

I don't know if that answered your question specifically or not.

Q. Well, your litigation packet, and the litigation packet is something that NMS produces in every single instance that it gets involved in cases like this, right?

A. Well, whenever we are requested. We do this quite often. We do this almost every day.

Q. Right. And what I think I hear you telling me is that the information in the data in your litigation packet, you are confident it's accurate.

A. Yes.

Q. Because you are confident in what NMS has done in this case and the information that NMS has

produced in this case.

A. Yes.

Q. But what you're ballparking is how that information should be interpreted.

A. Yes. Within the parameters of the case and the type of questions that you asked about that.

Q. Okay. So how would you describe your comfort level in taking the data that you are confident in and coming in and offering the ballpark opinion that you're, I guess, anticipating offering?

A. Well, based on the hypotheticals that Mr. Moriarty and I spoke about in terms of the time line, I'm comfortable to say, as I've said today, that it's my belief that at the time that Mrs. Johnson got sick, that her digoxin levels were elevated above what one may consider in the literature typical therapeutic levels.

That's as far as I'm comfortable with.

I'm not going to say -- give a specific number and say it was five times too high, it was two times too high. I can't do that.

I can just -- again, that's where I'm saying I'm ranging it and I'm ballparking it. But I'm comfortable with that statement.

Q. Okay. So we won't hear you offer an

opinion at trial to our jury other than, Ladies and gentlemen, it's my opinion that the digoxin was elevated, but I can't tell you how much it was elevated, I can't quantify it any better than that for you. Is that correct?

A. I may produce a number based on my calculations.

MR. MILLER: I just object to the form. I'm sorry to interrupt.

THE COURT REPORTER: Can you start your answer again? I'm sorry.

THE WITNESS: I'll state it again.

THE COURT REPORTER: Thank you.

THE WITNESS: I may quantify that based on the numbers and doing the rough calculations.

But I will offer an opinion and state that, you know, I can't be -- with any degree of reasonable scientific certainty that this number is a true number. Again, as I stated before.

That's why I'm saying I'm ranging and ballparking it.

Because we have an objective number that we're starting with in terms of the analytical data, and so we have some basis for doing some opinion.

Just like we would do in a DUI alcohol

case; we have a basis of a number and an opinion, and calculate back based on the facts of the case.

And that's what I would do.

BY MR. McPHAIL:

Q. So can you show me the rough calculations that you are going to show the jury on a piece of paper right there in front of you?

A. Well, sure. I mean, as I spoke, I would say, and we have -- this is what I've drawn based on Mr. Moriarty's and my discussion about the timing of the last dose being at 9:00 a.m. on the 26th, and about six hours later a peaking occurred about 3:00 p.m., and then she died about 24 hours at 4:00 p.m. on the 27th.

This was a hypothetical that we talked about.

So it's about 30 hours or so from the last dose to the death.

Now, the autopsy was taken out here, and of course the collection was out here sometime.

Q. Okay.

A. So what I would say is that we measure the value out here, okay.

And if we were to take -- make the assumption that there were no changes that occurred